Remarks

Claim Status

Claims 1, 5, 6, 26, 27, 102, 103, 105-107, 116 and 117 are pending. Claim 117 has been cancelled.

Applicants wish to thank the examiner for indicating that the rejection of claims 1, 5, 6, 26, 27, 102, 103, 105-107, and 116 as anticipated in view of U.S. Patent No. 4,548,925 has been withdrawn.

Applicants also wish to thank the examiner for the courtesy of an interview on June 18, 2007. Examiner Lundgren and the undersigned counsel discussed claim 1 in view of the Nicas reference, clarification of the term "at least one the substituent of the formula YXR", and the structure of the vancomycin core heptapeptide.

Rejection Under 35 U.S.C. §112, second paragraph

Claims 1, 5, 6, 26, 27, 102, 103, 105-107, and 116 stand rejected as allegedly being indefinite because, according to the examiner "it is not clear how the disaccharide group is attached to the vancomycin heptapeptide, and whether A4 corresponds to the chemical structure of natural vancomycin" (Action at 2).

Applicants respectfully traverse this rejection. Claim 1 states that the disaccharide group is "linked with a glycosidic bond" to the group A_4. The claim also clarifies that the claimed glycopeptide comprises "the formula A_1-A_2-A_3-A_4-A_5-A_6-A_7 [SEQ ID No.1] wherein the **groups A_1 to A_7 comprises the heptapeptide structure of**

naturally occurring vancomycin..." (emphasis added). These two points directly address the examiner's concerns.

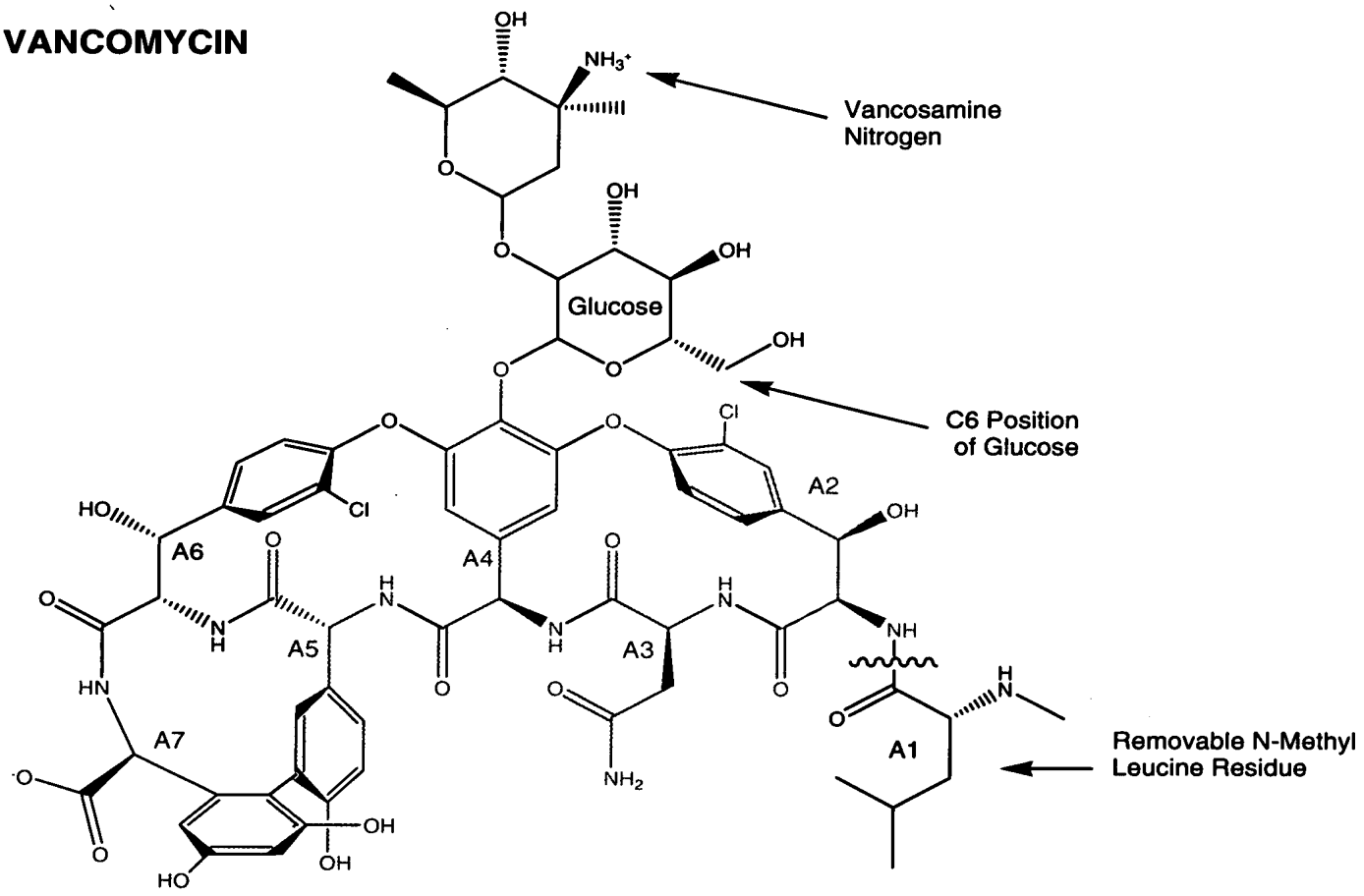
The specification supports this position and is instructive. For example, the specification teaches the conventional structural formula of vancomycin:

> The structural formula of vancomycin is shown below and is characterized by a disaccharide moiety covalently linked to a heptapeptide structure. The structure of vancomycin places it in a class of molecules referred to as the "dalbaheptides." Dalbaheptides in general are characterized by the presence of seven amino acids linked together by peptide bonds and held in rigid conformation by cross-links through the aromatic substituent groups of at least five of the amino acid residues. In the heptapeptide structure of vancomycin, which is commonly referred to as the "aglycone" of vancomycin, the aromatic side chains of amino acids 2, 4, and 6 are fused together through ether linkages. The side-chains of amino acids 5 and 7 are joined via a carbon-carbon bond. Amino acids 1 and 3 are leucine and asparagines, respectively. Other naturally occurring glycopeptide antibiotics are similar to vancomycin in that they have a glucose residue linked to the aromatic substituent on amino acid 4 through formation of a bond with a phenolic hydroxyl group.

(Specification at 2).

Below is the structural formula of naturally occurring vancomycin, with the amino acid groups A_1 through A_7 represented by color coding. (*See also*, Specification at 3).

VANCOMYCIN



It is well known in the glycopeptide art that the above representation is the structure of naturally occurring vancomycin. For example, Figure 1 of Nicas *et al.*, Antimicrobial Agents and Chemotherapy, 33(9):1477-1481 (1989) ("the Nicas reference"), relied on by the examiner to reject the pending claims as allegedly anticipated, shows the structure of vancomycin. Figure 1 of the Nicas reference is identical to the structure illustrated above (minus the color coding) and is identical to the vancomycin structure I appearing in Applicants' specification at page 3. Therefore, at least as early as the publication of the Nicas reference in 1989, the structure of vancomycin was established and known in the art.

Claim 1 is directed to a modified glycopeptide. It is composed of, *inter alia*, a heptapeptide (*i.e.*, 7 amino acids) that has the structure of naturally occurring vancomycin (i.e., the "aglycone" of vancomycin). Consequently then, A_4 is the naturally occurring vancomycin amino acid structure. Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §112 rejection for indefiniteness.

Claim rejections under 35 U.S.C. §112, first paragraph (enablement)

Claims 1, 5, 6, 26, 27, 102, 103, 105-107, and 116 stand rejected under 35 U.S.C. §112, first paragraph for alleged lack of enablement. Applicants traverse this rejection because the claims as written are enabled, and one skilled in the art would be able to make and use the invention. Independent claims 1 and 102 clearly define Applicants' invention. Claim 1 recites a "glycopeptide of the formula A_1-A_2-A_3-A_4-A_5-A_6-A_7, [SEQ ID NO:1] wherein the groups A_1 to A_7 comprise the **heptapeptide structure of naturally occurring vancomycin**..." (emphasis added) which is modified at the C6 position of the vancomycin glucose, thereby providing clarity to the claimed C6 modified vancomycin glycopeptides. Likewise, claim 102 recites a vancomycin glycopeptide antibiotic with glucose C6 modifications. It is noted that the Examiner admits that the specification "provides guidance and examples directed to the making and use (e.g. antibiotic) of vancomycin glucose C6 substituted derivatives." Action at 5. Therefore, Applicants submit that the pending claims are sufficiently enabled and request withdrawal of the rejection.

Claim rejections under 35 U.S.C. §112, first paragraph (written description)

Claims 1, 5, 6, 26, 27, 102, 103, 105-107, and 116 stand rejected under 35 U.S.C. §112, first paragraph for alleged lack of written description. Applicants traverse this rejection because the claims as written reasonably convey to one of skill in the art that Applicants were in possession of the invention. Claim 1 recites a "glycopeptide of the formula A_1-A_2-A_3-A_4-A_5-A_6-A_7, [SEQ ID NO:1] wherein the groups A_1 to A_7 comprise the heptapeptide structure of naturally occurring vancomycin..." which is modified at the C6 position of the vancomycin glucose, thereby providing clarity of the claimed vancomycin glycopeptides. Likewise, claim 102 recites a vancomycin glycopeptide antibiotic with glucose C6 modifications. These claims clarify that the invention encompasses modified vancomycin glycopeptides, which is adequately described throughout the specification, including as evident by the Table of synthesized compounds appearing at pages 131-135.

Applicants submit that it would be apparent to one of ordinary skill in the art that Applicants were in possession of the claimed invention at the time of filing, thereby fulfilling the requirements of the first paragraph of 35 U.S.C. §112. Withdrawal of the written description rejections is requested.

Rejection Under 35 U.S.C. §102(b)

Claims 1 and 5 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Nicas *et al.*, Antimicrobial Agents and Chemotherapy, 33(9):1477-1481 (1989) (the Nicas reference"). Applicants request withdrawal of this rejection in view of the amended claims. Claims 1 and 102 have been amended to more clearly define the invention. Claim 1 claims a "glycopeptide of the formula A_1-A_2-A_3-A_4-A_5-A_6-A_7, [SEQ

ID NO:1] wherein the groups A_1 to A_7 comprise the heptapeptide structure of naturally occurring vancomycin; and wherein the group A_4 is linked via a glycosidic bond to a disaccharide having a glucose residue directly attached to said A_4 residue, wherein said glucose residue bears an N-substituted aminohexose residue and at least one substituent of the formula YXR, attached to the C-6 position of said glucose; ... provided that at least one of **said** substituent of the formula YXR is not hydroxyl..." Claim 102 has been similarly modified. Support for this amendment can be found in the specification and claims as originally filed, as explained below.

As originally filed, the specification recited that "at least one of said sugar residues bears **one or more substituents of the formula** YXR, $N^+(R_1)=CR_2R_3$, $N=PR_1R_2R_3$, $N^+R_1R_2R_3$ or $P^+R_1R_2R_3$..." (See page 8, line 31 to page 9, line 1) (emphasis added). Similar language appeared in claim 1 as originally filed ("at least one of said sugar residues is a disaccharide modified to bear **one or more substituents of the formula** YXR, $N^+(R_1)=CR_2R_3$, $N=PR_1R_2R_3$, $N^+R_1R_2R_3$ or $P^+R_1R_2R_3$..."). The phrase "one or more substituents" was appropriately plural since it referred to the group of individual formulas YXR, $N^+(R_1)=CR_2R_3$, $N=PR_1R_2R_3$, $N^+R_1R_2R_3$ and $P^+R_1R_2R_3$, wherein each *formula* is a substituent, taken together to comprise the substituents.

Over the course of prosecution, claim 1 has been amended to delete reference to, *inter alia*, the substituents of formulas $N^+(R_1)=CR_2R_3$, $N=PR_1R_2R_3$, $N^+R_1R_2R_3$ and $P^+R_1R_2R_3$, leaving the formula YXR as the sole substituent. Thus, the group YXR should be considered as a whole to satisfy the term "substituent" and that term should now be used in the singular in claim 1.

Applicants recognize that the Examiner may be confusing another element of the claim language. Claim 1 also claims "at least *one or more* substituent of the formula YXR..." is attached to the glucose residue, indicating that at least one substituent of formula XYR is attached to the glucose residue, but more than one substituent of formula XYR may also be attached to the glucose. Claim 1 further provides a caveat, however, stating that "provided that at least one of **said** substituent of the formula YXR is not hydroxyl." This means that the formula XYR as a whole can not be hydroxyl. This claim language has been amended to further define the proper antecedent basis.

Claim 1 (and dependent claim 5) are therefore not anticipated by the Nicas reference. That reference teaches a modified vancomycin compound containing a substituted C6 glucose containing hydroxyl. Since Applicants' invention excludes a hydroxyl at this same position, Nicas can not be said to anticipate each and every limitation of the claimed invention.

Conclusion

Applicants submit that claims 1, 5, 6, 26, 27, 102, 103, 105-107, 116, and 117 are in condition for allowance. An early Notice of Allowance is respectfully requested. If the Examiner disagrees, he is invited to telephone the undersigned.

Date: June 18, 2007

Angela Verrecchio
Registration No. 54,510

Woodcock Washburn LLP
Circa Centre- 12th Floor
2929 Arch Street
Philadelphia PA 19104-2891
Telephone: (215) 568-3100
Facsimile: (215) 568-3439